

Claims:

1. A metalloprotease having an aggrecanase activity, which comprises an amino acid sequence of from the 213th position to the 583rd position of an amino acid sequence represented by SEQ ID NO:1 or which consists of an amino acid sequence of from the 213th position to the 583rd position of the amino acid sequence represented by SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted.

2. A metalloprotease having an aggrecanase activity, which comprises an amino acid sequence of from the 1st position to the 583rd position of an amino acid sequence represented by SEQ ID NO:1 or which consists of an amino acid sequence of from the 1st position to the 583rd position of the amino acid sequence represented by SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted.

3. A metalloprotease having an aggrecanase activity, which consists of an amino acid sequence represented by SEQ ID NO:1, an amino acid sequence of from the 1st position to the 687th position of an amino acid sequence represented by SEQ ID NO:1, an amino acid sequence of from the 1st position to the 583rd position of the amino acid sequence represented by SEQ ID NO:1, an amino acid sequence of from the 213th position to the 950th position of the

amino acid sequence represented by SEQ ID NO:1, an amino acid sequence of from the 213th position to the 687th position of the amino acid sequence represented by SEQ ID NO:1 or an amino acid sequence of from the 213th position to the 583rd position of the amino acid sequence represented by SEQ ID NO:1, or any one of these sequences wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted.

4. A gene which encodes an amino acid sequence of the metalloprotease having an aggrecanase activity described in any one of claims 1 to 3.

5. A vector which comprises the gene described in claim 4.

6. A host cell which comprises the vector described in claim 5.

7. A method for producing the metalloprotease having an aggrecanase activity described in any one of claims 1 to 3, which comprises using the host cell described in claim 6.

8. An antibody against the metalloprotease having an aggrecanase activity described in any one of claims 1 to 3.

9. A method for screening a substance capable of inhibiting an aggrecanase activity of a metalloprotease, which comprises allowing the metalloprotease having an aggrecanase activity described in any one of claims 1 to 3 to contact with a compound to be tested.

10. A pharmaceutical composition for inhibiting degradation of proteoglycans, which comprises a substance capable of inhibiting the metalloprotease having an aggrecanase activity described in any one of claims 1 to 3, as an active ingredient.

11. A gene represented by SEQ ID NO:24, 25, 26, 27, 28, 29, 30 or 31, or a gene represented by SEQ ID NO:24, 25, 26, 27, 28, 29, 30 or 31 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, which has a joint disease aggrecanase promoter activity.

12. An antibody against a metalloprotease having aggrecanase activity, wherein said metalloprotease is selected from the group consisting of:

(a) a purified metalloprotease comprising an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted,

deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(b) a purified metalloprotease comprising an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(c) a purified metalloprotease comprising an amino acid sequence selected from the group consisting of an amino acid sequence represented by amino acids 1-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1, and any one of said sequences wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity; and

(d) a purified metalloprotease comprising an amino acid sequence that has 90% or more sequence homology with the amino acid sequence set forth in SEQ ID NO:1, wherein said metalloprotease has aggrecanase activity.

13. A method for screening a substance capable of inhibiting an aggrecanase activity of a metalloprotease, which comprises allowing the metalloprotease to contact a compound to be tested, wherein the metalloprotease is selected from the group consisting of:

(a) a purified metalloprotease comprising an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(b) a purified metalloprotease comprising an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(c) a purified metalloprotease comprising an amino acid sequence selected from the group consisting of an amino acid sequence represented by amino acids 1-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-950 of

SEQ ID NO:1, an amino acid sequence represented by amino acids 213-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1, and any one of said sequences wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity; and

(d) a purified metalloprotease comprising an amino acid sequence that has 90% or more sequence homology with the amino acid sequence set forth in SEQ ID NO:1, wherein said metalloprotease has aggrecanase activity.

14. A pharmaceutical composition for inhibiting degradation of proteoglycans, which comprises a substance capable of inhibiting a metalloprotease selected from the group consisting of:

(a) a purified metalloprotease comprising an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(b) a purified metalloprotease comprising an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 1-583 of SEQ ID

NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(c) a purified metalloprotease comprising an amino acid sequence selected from the group consisting of an amino acid sequence represented by amino acids 1-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1, and any one of said sequences wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity; and

(d) a purified metalloprotease comprising an amino acid sequence that has 90% or more sequence homology with the amino acid sequence set forth in SEQ ID NO:1, wherein said metalloprotease has aggrecanase activity.

15. A method of treating a joint disease, comprising administering to a patient in need of treatment a compound obtainable by the method of claim 13, thereby treating a joint disease.

16. A polynucleotide represented by SEQ ID NO:24, 25, 26, 27, 28, 29, 30 or 31, or a polynucleotide represented by SEQ ID NO: 24, 25, 26, 27, 28, 29, 30 or 31 and, wherein from 1 to 10 nucleotide residues are substituted, deleted and/or inserted, wherein said polynucleotide has a joint disease aggrecanase promoter activity.

17. A method for screening a substance capable of inhibiting aggrecanase promoter activity, which comprises allowing a cell transformed with the polynucleotide described in claim 16 to contact a compound to be tested.